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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,171	01/03/2002	Robert Haley	UTSD:749US	7156

7590 04/20/2007

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/039,171	HALEY ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5,9-25,36-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-25,36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 9-25 and 36-43 are pending.

Election/Restrictions

The election/restriction is moot in view of the cancellation of claims directed to non-elected inventions and as stated in the previous office action, claims 2 and 22 are rejoined with elected invention and examined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Instant invention read on a method of delivering an expression cassette comprising a promoter operably linked to a gene encoding PON1 to a cell either in vitro or in vivo, wherein said expression cassettes expresses PON1 in said cell providing protection from said organophosphate (OP) toxin. The claimed method does not require the active step of the cells being exposed to an OP toxin.

Claims 1-5, 10-13, 17-25, 37-39 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Radtke (US 6,521,226). Radtke teaches, "More specifically, the invention is

directed to a method of decreasing atheroma formation in mammals, by administration of paraoxonase-1 (PON-1), an expressed protein that has hydrolase activity for organophosphate, and antioxidation activity for low-density lipoprotein (LDL)." See columns 1 and 15-16. Radtke teaches that PON1 type R and Q are known variants in humans and can be used in the method (columns 4-5 and 15-16). Radtke teaches using PON 1 in gene therapy using a number of viral vectors comprising and methods of delivery are known in the prior art (column 8-9). PON1 type Q phenotype has been correlated with higher paraoxonase activity than the type R phenotype (column 8). An assay can be used to measure either phenotype or the ratio of the two phenotypes present in an individual (column 8).

Although Radtke is silent with respect to the limitations "providing protection from said organophosphate toxin" in instant claims 1 and 21 and the limitations "said cassette increase PON1 type Q (R) expression by about 10-fold" in the instant claims 17 and 18, Radtke anticipates all of the claimed active method steps, so the function effects of the claimed methods are considered to be inherent in the method steps taught by Radtke.

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare

prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Applicant's arguments, see pages 7-8, filed 2/6/07, with respect to the rejection(s) of claim(s) 1-5, 9-15, 17-25 under 102(b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Radtke et al (US 6,521,226).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9, 14-16, 21, 36, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radtke (US 6,521,226) taken with Scheffler (US 5,721,118). Radtke teaches, "More specifically, the invention is directed to a method of decreasing atheroma formation in mammals, by administration of paraoxonase-1 (PON-1), an expressed protein that has hydrolase activity for organophosphate, and antioxidation activity for low-density lipoprotein (LDL)." See columns 1 and 15-16. Radtke teaches that PON1 can be used in gene therapy using a number of viral vectors and methods of delivery known in the prior art (column 8-9). However, Radtke does not specifically teach using a polyadenylation (poly A) tail in the vector.

However, at the time the invention was made, one of ordinary skill in the art understands that poly A tail protects mRNA molecule from exonucleases and is important for transcription termination, for export of the mRNA from the nucleus and for translation. Scheffler teaches using poly A tail for regulating gene expression (column 5). In addition, tissue-specific, constitutive, and inducible promoters for expressing a gene of interest were well known to one of ordinary skill in the art as exemplified by Scheffler (column 6).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Radtke taken with Scheffler, namely to make and use a poly A tail in the vector in the method. One of ordinary skill in the art would have been motivated to combine the teaching for protecting the mRNA from exonucleases and for proper polyadenylation of the gene transcript.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Radtke taken with Scheffler, namely to make and use a promoter selected from a constitutive promoter, an inducible promoter, or a tissue specific promoter in the vector in the method. One of ordinary skill in the art would have been motivated to combine the teaching for properly or efficiently expressing the DNA encoding PON1 in a desired cell.

In view of the teaching of Radtke and Scheffler, one of ordinary skill in the art would have had a reasonable expectation of success for practicing the method because the promoter were well known to one of ordinary skill in the art for expressing a heterologous nucleic acid in a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 7-8, filed 2/6/07, with respect to the rejection(s) of claim(s) 1 and 19 under 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Radtke and Murphy. Applicant argues that the evidence of record would overwhelmingly support the conclusion that one skilled in the art would find the present claims enabled (see pages 9 and 14 of applicant's arguments filed on 11/17/06).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764.

The examiner can normally be reached on Monday through Friday from 6:30 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Douglas Schultz, PhD, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Brian Whiteman